**Standardizing Clinical Abstracts - Patients' Perspective**

**An Opportunity to Inform Public Understanding and Foster Expert Analysis**

Clinical research – by the nature of how it's reported in abstracts – is not informing public beliefs or understanding – or fostering efficient analysis of this vital work among experts.

Here we propose and ask if the medical journals could develop standard formats for clinical abstract reporting – requiring the clear reporting of key findings, complementary to the National Institutes of Health goal to expand the Clinical Trials Registry and Results Database.[1]

It may be argued that the intended audience is not the patient community or the public at large – that clinical abstracts are informal summaries by and for scientists, similar to conversation. There's validity to this perspective, but also hidden costs and many missed opportunities, described within. Further, we note that patients, as the primary subjects of clinical research, should not be excluded unnecessarily from the conversation.

> "Ethical clinical research should contribute to generalizable knowledge and improve human health. The dedication of patients who take the risks to participate in clinical research is dishonored when their data remain secret." - Alastair J.J. Wood, M.D [2]

Most individuals when initially diagnosed with a cancer have little or no medical background or training in drug assessments or scientific method. Nor do we have access to the full text as published in medical journals. However, the abstracts describing this research are widely available to patients on the Internet or through press releases.

- Patients, facing life-threatening disease, want to know what these studies mean, suggest, or prove in order to make more informed clinical decisions. So we (a patient group) are often asked to help interpret clinical abstracts – or to comment on media interpretations.

- This is a task we approach cautiously, because of our own limitations, but also because abstracts are published in a variable manner, typically as dense and complex strings of text in highly technical language. Further, many details and relationships (key to a fair assessment) may only exist in the full report; and the basic principles of how clinical evidence is weighed will not be found even in the full text of published papers.

Faced with media-born misinformation and conflicting interpretations even among professionals, the public may lose trust in the clinical research process. Patient and physician analysis will be based on incomplete information – rambling text. Public belief will be based on happenstance – acquired from untrained parents, an influential friend, the claims made in shock media, a best-selling book or popular website – making patient/physician shared decision-making more challenging than it needs to be.

In such an environment, we have observed that one report can be, unwisely, considered equivalent to any other. That is, we may trust specific clinical trial reports too much or too little, or embrace them too selectively … based on what we want to be true, or based on the faith we have in certain individuals or institutions – or we may unwisely mistrust any study funded by a drug company or

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[1] http://grants.nih.gov/grants/guide/notice-files/not-od-09-077.html

[2] Wood, Alastair J.J.
**Progress and Deficiencies in the Registration of Clinical Trials**
N Engl J Med 2009 360: 824-830

the government.

To address the confusion, we ask if a structured abstract format could be required for clinical reports submitted to the medical journals – with a focus on the elements of clinical research that are **key to assessment by the FDA**. Noting that one need not have a deep understanding of the biology of the disease, or the mechanisms of a drug to appreciate which studies provide strong or weak evidence of meaningful clinical benefit if you show the key findings, side by side.

In **Table 1** we provide our draft proposal: a **Tabular** format with required **Elements** in **Logically** determined **Locations** (or **TELL**). In **Table 2**, we propose explanations of TELL elements for the public and media.

To those who may worry about the increased space requirements of a TELL-like format and the associated costs, we note that improving the clarity of clinical abstracts seems an excellent tradeoff:

- Enhance the ability of the scientific community to filter and weigh reports, and compare results across different journals.
- Help sponsors and clinical investigators to make better decisions when designing clinical studies.
- Be a deterrent against intentional or unintentional sponsor/investigator bias and common media-born misinformation.
- Discourage reporting of clinical data that has not yet matured.
- Help build public confidence in the objectivity of clinical science.
- Provide a stronger basis for informed consent among patients and their treating physicians when considering clinical trials.
- Foster more objective judgments among investors about which candidate drugs have the most potential, helping to attract needed capital to the more deserving inventions, while letting the less promising agents fail faster.
- By providing universal templates for abstracts the authors may well produce higher quality abstracts more efficiently.
- And, as noted, such reporting would be complementary to the NIH initiative to expand the Clinical Trials Registry and Results Database. The results could be efficiently ported, one to the other.

Finally, in FDA drug advisory committee reviews we have observed that the decision to approve or deny applications for FDA marketing approval hinges on the relationships between outcome events and background detail, such as included in TELL. Such information is rarely if ever proprietary and in need of protection. As your readers know, the full text of the published paper could exclusively provide the more technical background, such as on the biology of the diseases and presumed mechanisms of action of the investigational agents, supporting productive conversation among scientists and progress against human disease.

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# TABLE 1

| Elements | Proposed TELL format:<br>Required Elements for CLINICAL Research Abstracts |
|---|---|
| **N**<br><br>Evaluated / Intent to Treat | Number of participants in the clinical trials (Evaluated / Intent to Treat).<br><br>We propose that intent to treat be included in all clinical research abstracts, expressed as: N = Evaluated / ITT. Example: N = 300/500 |
| **Population**<br><br>(Clinical circumstance) | Medical condition (and subtypes):<br>Risk: High, medium, low risk<br>Performance index \| Prognostic index<br><br>Number and Type of Prior Therapies,<br>Median age \| Genetic characteristics |
| **Primary Clinical Questions** | Key endpoints, such as:<br><br>Safety \| Overall response rate \| CR rate,<br>Progression Free Survival, \| Survival … |
| **Study Type** | Phase:<br>Randomized / Single arm<br>Prospective / subset analysis |
| **Methods: Protocol** | Brief outline of therapeutic protocols and how they were administered (oral, IV, continuous infusion) over time. |
| **Methods: Assessment** | Summary of how outcomes were measured, such as:<br><br>Independent / Investigator<br>Schedule (weekly, monthly)<br>Type (blood, imaging) |
| **Maturation** | Completed / Interim?<br>Time to enrollment and analysis? |
| **Efficacy Results** | As defined in Primary Clinical Questions<br><br>Expressed as Rate, include Confidence range, such as:<br>Evaluated: CR/n (%) (CI range)<br>Intent to Treat: CR/n (%) (CI range) |
| **Safety Results** | Expressed as rate with range:<br>By grade (severity): Serious first.<br>For Evaluated: SE/n (%) (CI range)<br>For ITT – if toxicities led to dropping out |
| **Mortality** | Death rate:<br>On study \| Off Study<br>Evaluated \| Intent to Treat<br>Expected rate in this population: |
| **Limitations** | Authors describe limitations of the study methods and design – such as sample size, or study type … to describe level of evidence and if findings are consistent with other studies |
| **Discussion** | Free text area. Authors might provide here the implications of the findings – interpretations, and other information and background that do not fit in the clinical results fields. |

# TABLE 2

| Elements | Explanations of TELL elements, not included in abstracts but available on the Internet for the public and media (draft). |
|---|---|
| **N**<br><br>Evaluated / Intent to Treat | N stands for the number of participants. Was it defined up front, or was it arbitrary – based on how many could be enrolled?<br><br>N provides the denominator - a reference point for estimating the results in the real world.<br><br>A meaningful denominator is missing in case reports / testimonials – which is why such reports are considered anecdotal - not evidence of causality or predictive of outcomes in others.<br><br>Study results from a pre-defined (prospectively defined) N provide more confidence than N determined by chance, circumstances, or investigator ad hoc decisions.<br><br>Intent to Treat (ITT) accounts for all participants that enrolled in the study, not just those who completed the protocol and were available for evaluation. When the ITT is greater than the number Evaluated, it calls into question the integrity of the analysis. |
| **Population**<br><br>(Clinical circumstance) | How scientists and regulators interpret the results of a study is dependent on the population – the natural history of the disease untreated, or treated differently, but also the characteristics and performance of the participants. Did the study population have low or high-risk disease? For example, response rates in the previously untreated lymphoma patients can be more difficult to interpret than in those who have received many prior therapies. |
| **Primary Clinical Questions** | Endpoints describe what is being measured to determine if the intervention provided meaningful clinical benefit – net benefit or harm.<br><br>Of the measures used in clinical research, **Survival** is considered the most reliable as it accounts for measured and unmeasured effects. However, survival differences cannot always be measured for conditions that have a long clinical course, especially where other treatments will confound assessment … was it improved by the first or last treatment? |
| **Study Type** | Randomized studies provide the most objective basis for identifying and comparing risks and benefits, relative to the control therapy – typically the standard of care. |
| **Methods: Protocol** | Patients will want to know how the drug is administered: orally, by IV, by continuous infusion, and the duration of treatment. |
| **Methods: Assessment** | Notably, Independent data monitoring is often used in pivotal phase III trials to guard against biased interpretations, and to provide consistent evaluation methods. |
| **Maturation** | Even after a study has completed the administration phase, many months or years may be needed to measure the endpoints, such as time to progression or other events being measured in the study. |
| **Efficacy Results** | To most accurately calculate the response rates in the study population requires a pre-defined defined denominator (N), which is the basis for estimating the rates for study drug effects in the general population. |
| **Safety Results** | Notably, case reports and testimonials, lacking a denominator, cannot be used to determine the cause of the outcome or how likely it will occur in others. If the ITT is much larger than the analysis group, it's important to ask why. |
| **Mortality** | Mortality events can be acceptable in a population with high-risk disease. |
| **Limitations** | Reproducibility is the cornerstone of confidence in clinical outcomes – the objective assessment of risks and benefits.<br><br>Size (N) counts, but having a second group achieve similar findings makes error (false negatives or positives) less likely.<br><br>Randomized studies protect against patient selection bias and provide a reliable control to compare benefits and risks. |
| **Discussion** | Experts have noted that the conclusions of research authors are prone to bias. |